Remarks

Introduction

Claims 21, 38, 41, and 51 were pending. By way of this response, claim 38 has been amended. Support for the amendments to claim 38 can be found in the application as originally filed, and no new matter has been added. Accordingly, claims 21, 38, 41, and 51 remain pending.

Claim Objections

Claims 38 have been objected to for being of improper dependent form.

Claim 38 has been amended to be dependent from claim 21 as suggested in the Office Action. Therefore, applicant submits the objection has been overcome.

Specification Objections

The specification has been objected to because the Cross-Reference section did not include the current status of the priority documents.

The paragraph beginning at page 1, line 4 has been amended as set forth above. Applicant submits the objection has been overcome.

Rejections Under 35 U.S.C. § 103

Claims 21, 38, 41, and 51 have been rejected under 35 U.S.C. § 103 as allegedly being unpatentable over Borodic (U.S. Patent No. 5,183,462) in view of Davis et al. (Movement Disorders, July 1993; hereinafter Davis). The Office Action states that it would be obvious to use botulinum toxin type B, presumably as disclosed by Borodic, to treat pain of lower back muscles, as disclosed by Davis.

Applicant respectfully disagrees and traverses the rejections. Among other things, applicant does not agree that Davis is prior art to the above-identified application. Davis was published in July 1993, and the above-identified application has an effective filing date of December 28, 1993. Applicant reserves the right to antedate Davis in the future at applicant's discretion.

In addition, applicant submits that a *prima facie* case of obviousness has not been established because a person of ordinary skill in the art would not be motivated to combine the teachings of Borodic with the teachings of Davis. Moreover, even if Borodic could erroneously be combined with Davis, the combination fails to disclose, teach, or suggest all of the limitations of the claims.

Applicant submits that a person of ordinary skill in the art would not be motivated to combine the teachings of Borodic with the teachings of Davis.

To support applicant's position, and as evidence supporting the unobviousness and patentability of the present claims, applicant submitted a copy of the February 8, 2001 declaration of Dr. Mitchell Brin (hereinafter the Brin Declaration) with the Preliminary Amendment filed on June 18, 2001,. In the Office Action, the Examiner appears to have not taken into consideration the evidence presented by way of the Brin Declaration.

The Brin Declaration Rebuts the Obviousness Rejection

A copy of the Brin Declaration is being resubmitted with this response.

Decisions from the courts, which review patent office decisions, are instructive as to the deference and weight to be accorded the evidence presented in the Brin Declaration. An expert opinion expressed in a Declaration can overcome an obviousness rejection: "The expert opinion was introduced on the issue of the level of ordinary skill … the prima facie case of obviousness has been overcome", and the Examiner's obviousness rejection was reversed. *In re Oelrich and Divigard*, 579 F.2d 86, 198 USPQ 210 at 215 (CCPA 1978).

Additionally, in *In re May and Eddy*, 574 F.2d, 197 USPQ 601 (CCPA 1978), four declarations were submitted in response to an obviousness rejection. The Court relied heavily upon the affidavit from an expert in the field (the Jackson affidavit) which stated that the claimed method of affecting analgesic and morphine antagonistic activity through use of a particular compound "was unexpected and unpredictable" since the property

of the compound used in the method to affect analgesic and morphine antagonistic activity "had not previously been established." (197 USPQ at 606) (emphasis added). The Court concluded based in large part upon the Jackson affidavit (see 197 USPQ 608, paragraph [6]) that the method claims were not obvious, and reversed the Examiner's obviousness rejection. *In re May and Eddy* is directly applicable here since the present claims are method claims (treatment of pain associated with a muscle disorder), which use a particular compound (botulinum toxin type B).

The original of the Brin declaration was submitted in related U.S. Application Serial Number 09/490,756 with the response dated February 16, 2001. Dr. Brin is an acknowledged expert in the use of botulinum toxin for treating neuromuscular disorders.

Paragraph 6 of the Brin declaration states: "As of the April 25, 1991 date of the Jankovic reference, it was **completely unknown** as to whether or not botulinum toxin type B would have any therapeutic efficacy in humans. Indeed, as far as I am aware, the first reported use of type B botulinum toxin in humans did not occur until 1995" (emphasis added).

Additionally, paragraph 8 of the Brin declaration states: "In my opinion, prior to December 28, 1993, it would have been **foolhardy and dangerous** to use botulinum toxin type B to treat patients with dystonia, such as cervical dystonia, in light of clinical experience with the type B toxin as of that date" (emphasis added).

The Brin declaration has been submitted as evidence that the claims in this application are in condition for allowance, that is that the claims are unobvious from and patentable over the prior art. In other words, since there had been no use of botulinum toxin type B to treat any disease condition prior to the effective filing date of the present application (i.e., December 28, 1993) and based upon the additional evidence presented by the Brin declaration, the present claims (claims 21, 38, 41, and 51), directed to the use of botulinum toxin type B to treat pain associated with a muscle disorder, are free of the art and are in condition for allowance.

Note that as set forth in the Brin declaration, the first reported use of botulinum toxin type B (to which the present claims are directed) to treat any ailment was not until 1995. Hence, it follows that it would have been **"foolhardy and dangerous"** to use botulinum toxin type B to treat pain associated with a muscle disorder in a patient prior to the December 28, 1993 effective filing date of the instant application.

In view of the above, applicant submits that the present claims are unobvious and patentable over the prior art as cited in the Office Action.

Furthermore, applicant submits that a person of ordinary skill in the art would not be motivated to combine Borodic and Davis because Borodic does not disclose, teach, or even suggest the use of any neurotoxin, let alone botulinum toxin type B, to treat back pain, as acknowledged in the Office Action.

In addition, applicant submits that a *prima facie* case of obviousness has not been established because the combination of Borodic and Davis fails to teach or suggest all of the elements of the present claims.

Applicant submits that Borodic does not disclose, teach, or suggest the present invention. For example, Borodic does not disclose, teach, or even suggest the use of botulinum toxin type B at all, let alone the use of botulinum toxin type B to treat pain. In fact, Borodic does not even mention botulinum toxin type B, let alone disclose or suggest the use of botulinum toxin type B as a therapeutic agent. In contrast, Borodic states that the invention relates to a method for controlled administration of chemodenervating agents (Abstract). Borodic further states that the invention is unlimited with respect to the nature of the neurotoxin, and that the neurotoxin may take the form of any of the known types of botulinum toxin (A through G) or various engineered proteins which retain the native form's ability to block acetylcholine release (column 3, lines 51-61). In addition, Borodic states that many neurotoxins are known (column 4, lines 52-53). The only description of any neurotoxin in Borodic is of botulinum toxin type A.

Davis fails to make up for the deficiencies of Borodic. For example, Davis only discloses that botulinum toxin type A can result in a cessation of pain. Davis does not disclose, teach, or even suggest using any other neurotoxin, let alone botulinum toxin type B, as recited in the present claims.

The mention of botulinum toxin (A through G) identified by the Examiner at column 3, lines 58-61 of Borodic relates to

seven different chemodenervating agents among a lengthy list of various other agents, such as engineered proteins and other neurotoxins that may be employed in the methods disclosed by Borodic. As stated above, botulinum toxin type B is not even specifically mentioned by Borodic.

The motivation or suggestion to support a rejection under 35 U.S.C. § 103 must be clear and particular (*In re Dembiczak*, 175 F.3d 994, 999, 50 USPQ2d 1614, 1617 (Fed. Cir. 1999); emphasis added), and "particular findings must be made as to the reason the skilled artisan, with no knowledge of the claimed invention, would have selected these components for combination in the manner claimed" (*In re Kotzab*, 217 F.3d 1365, 1371, 55 USPQ2d 1313, 1317 (Fed. Cir. 2000)). Applicant respectfully submits that the prior art fails to provide a clear and particular showing that one of ordinary skill in the art would have been motivated to combine the deficient teachings of Borodic and Davis, let alone to combine them and obtain the claimed methods.

Applicant submits that the listing of many different chemodenervating agents, including neurotoxins and engineered proteins, of Borodic provides no more than speculation of potential types of agents that can be used in the method of controlling administration of chemodenervating agents of Borodic. The listing does not provide any motivation or incentive to a person of ordinary skill in the art to combine Borodic and Davis, let alone to combine Borodic and Davis and select botulinum toxin type B to treat pain, as recited in the present claims.

Applicant submits that, based on the teachings of Borodic and Davis, alone or in any combination, a person of ordinary skill in the art would still be required to guess, test, speculate, and/or arbitrarily "pick and choose" a specific chemodenervating agent (e.g., botulinum toxin type B) from among the long list of different agents identified by Borodic, let alone to do so and further to administer that agent to a patient to treat pain, as recited in the present claims. Borodic does not place any significance whatsoever in the types of botulinum toxin other than type A relative to the other agents disclosed.

Simply put, the brief mention in Borodic of botulinum toxin (A through G) in a long list of other, different chemodenervating agents, is insufficient for Borodic, alone or in any combination with Davis, to teach or suggest the methods recited in the presently rejected claims. For example, the brief mention of botulinum toxin (A through G) is insufficient for Borodic, alone, or in combination with Davis, to teach or suggest the use of botulinum toxin type B to treat pain.

Only after knowing of applicant's invention and disclosure would one of ordinary skill in the art select botulinum toxin type B from among the many other different chemodenervating agents disclosed by Borodic, and use such botulinum toxin type B to treat pain, as recited in the present claims. Applicant submits that such hindsight is an improper basis for rejecting patent claims.

Therefore, in view of the above, applicant submits that the present claims, that is claims 21, 38, 41, and 51, are unobvious

from and patentable over Borodic and Davis, alone or in any combination, under 35 U.S.C. § 103.

In addition, each of the present dependent claims is separately patentable over the prior art. For example, none of the prior art disclose, teach, or even suggest the present methods including the additional feature or features recited in any of the present dependent claims. Therefore, applicant submits that each of the present claims is separately patentable over the prior art.

Conclusion

In conclusion, applicant has shown that the present specification is in proper form, that the present claims are not anticipated by and are unobvious from and patentable over the prior art under 35 U.S.C. §§ 102 and 103. Therefore, applicant submits that the present claims, that is claims 21, 38, 41, and 51 are allowable. Therefore, applicant respectfully requests the Examiner to pass the above-identified application to issuance at an early date. Should any matters remain unresolved, the Examiner is requested to call (collect) applicant's attorney at the telephone number given below.

Respectfully submitted,

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